DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Dr. Rolland D. Carlson
General Manager, Divisional Vice President
Vysis, Inc.
3100 Woodcreek Dr.
Downers Grove, IL 60515

DEC 13 2004

Re: K041875
Evaluation of Automatic Class III Designation
Vysis® AutoVysion™ System
Regulation Number: 21 CFR 866.4700
Classification: Class II
Product Code: NTH

Dear Dr. Carlson:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your petition for classification of the Vysis® AutoVysion™ System that is intended for in vitro diagnostic use with the Vysis® PathVysion® HER-2 DNA Probe Kit to aid in the detection and enumeration of FISH signals in interphase nuclei, and to determine the LSIB HER-2 to CEPB 17 signal ratio of the HER-2/*neu* gene via FISH in formalin-fixed, paraffin-embedded human breast cancer tissue specimens; to reduce overall hands-on time by performing automated enumeration (for a small percentage of samples [less than 7%] manual enumeration may be required); as an adjunctive computer-assisted methodology to assist in the acquisition and measurement of images from microscope slides of formalin-fixed, paraffin-embedded breast cancer tissue sections for the presence of amplified HER-2/*neu* gene and as an aid in determining HER-2/*neu* amplification status, in conjunction with optional manual visualization directly through the fluorescence microscope.

FDA concludes that this device, and substantially equivalent devices of this generic type, should be classified into class II. This order, therefore, classifies the Vysis® AutoVysion™ System, and substantially equivalent devices of this generic type into class II under the generic name, Automated Fluorescence in situ Hybridization (FISH) Enumeration Systems. This order also identifies the special controls applicable to this device.

FDA identifies this generic type of device as:

21 CFR 866.4700 Automated Fluorescence in situ Hybridization (FISH) Enumeration Systems. An automated FISH enumeration system is a device that consists of an automated scanning microscope, image analysis system and customized software applications for FISH assays. This device is intended for in vitro diagnostic use with FISH assays as an aid in the detection, counting and classification of cells based on recognition of cellular color, size and shape and in the detection and enumeration of FISH signals in interphase nuclei of formalin-fixed, paraffin-embedded human tissue specimens.

In accordance with section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360c(f)(1)) (the act), devices that were not in commercial distribution prior to May 28, 1976 (the date of enactment of the Medical Device Amendments of 1976 (the amendments)), generally referred to as postamendments devices, are classified automatically by statute into class III without any FDA rulemaking process. These devices remain in class III and require premarket approval, unless and until the device is classified or reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act (21 U.S.C. 360c(i)), to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and Part 807 of the FDA regulations (21 CFR 807).

Section 513(f)(2) of the act provides that any person who submits a premarket notification under section 510(k) for a device may, within 30 days after receiving an order classifying the device in class III under section 513(f)(1), request FDA to classify the device under the criteria set forth in section 513(a)(1). FDA shall, within 60 days of receiving such a request classify the device. This classification shall be the initial classification of the device type. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the **Federal Register** classifying the device type.

On October 13, 2004, FDA filed your petition requesting classification of the Vysis® AutoVysion™ System into class II. The petition was submitted under section 513(f)(2) of the act. In accordance with section 513(f)(1) of the act, FDA issued an order on October 1,2004, automatically classifying the VysisB AutoVysion™ System in class III, because it was not within a type of device which was introduced or delivered for introduction into interstate commerce for commercial distribution before May 28, 1976, which was subsequently reclassified into class I or class II. In order to classify the VysisB AutoVysion™ System into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use.

After review of the information submitted in the petition, FDA has determined that the VysisB AutoVysion™ System, intended for in vitro diagnostic use with the VysisB PathVysion® HER-2 DNA Probe Kit to aid in the detection and enumeration of FISH signals in interphase nuclei, and to determine the LSI® HER-2 to CEP® 17 signal ratio of the HER-2/*neu* gene via FISH in formalin-fixed, paraffin-embedded human breast cancer tissue specimens; as an adjunctive computer-assisted methodology to assist in the acquisition and measurement of images from microscope slides of formalin-fixed, paraffin-embedded breast cancer tissue sections for the presence of amplified HER-2/*neu* gene and as an aid in determining HER-2/*neu* amplification status, in conjunction with optional manual visualization directly through the fluorescence microscope can be classified in class II with the establishment of special controls. FDA believes that class II special controls provide reasonable assurance of the safety and effectiveness of the device.

FDA has identified no direct risks to health related to use of automated FISH enumeration systems. However, failure of the system to perform as indicated, could lead to inaccurate results that could

result in misdiagnosis, inappropriate treatment and improper patient management. The measures FDA recommends to mitigate these risks are described in the guidance document, "Class II Special Controls Guidance Document: Automated Fluorescence *in situ* Hybridization (FISH) Enumeration Systems", which includes recommendations for performance validation and labeling.

In addition to the general controls of the act, this device type is subject to the following special controls: "Class II Special Controls Guidance Document: Automated Fluorescence *in situ* Hybridization (FISH) Enumeration Systems". Section 510(m) of the act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device and, therefore, the device is not exempt from the premarket notification requirements. Thus, persons who intend to market this type device must submit to FDA a premarket notification submission containing information on the Automated Fluorescence *in situ* Hybridization (FISH) Enumeration Systems they intend to market prior to marketing the device.

A notice announcing this classification order will be published in the **Federal Register. A** copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market this device, subject to the general control provisions of the act and the special controls identified in this order. If you have any questions concerning this classification order, please contact Maria Chan at (240) 276-0493 ext. 130.

Sincerely yours,

Steven Gutman, M.D.

Steven I. Gutman, M.D., M.B.A.
Director
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health